The inflammatory sequelae of aortic balloon occlusion in hemorrhagic shock

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ARTICLE INFO

ABSTRACT

Background: Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a hemorrhage control and resuscitative adjunct that has been demonstrated to improve central perfusion during hemorrhagic shock. The aim of this study was to characterize the systemic inflammatory response associated and cardiopulmonary sequelae with 30, 60, and 90 min of balloon occlusion and shock on the release of interleukin 6 (IL 6) and tumor necrosis factor alpha.
Materials and methods: Anesthetized female Yorkshire swine (*Sus scrofa,* weight 70 90 kg) underwent a 35% blood volume controlled hemorrhage followed by thoracic aortic balloon occlusion of 30 (30 REBOA, $n = 6$), 60 (60 REBOA, $n = 8$), and 90 min (90 REBOA, $n = 6$). This was followed by resuscitation with whole blood and crystalloid over 6 h. Animals then underwent 48 h of critical care with sedation, fluid, and vasopressor support.
Results: All animals were successfully induced into hemorrhagic shock without mortality. All groups responded to aortic occlusion with a rise in blood pressure above baseline values. IL 6, as measured (picogram per milliliter) at 8 h, was significantly elevated from baseline values in the 60 REBOA and 90 REBOA groups: 289 ± 258 *versus* 10 ± 5; $P = 0.018$ and 630 ± 348; $P = 0.007$, respectively. There was a trend toward greater vasopressor use ($P = 0.183$) and increased incidence of acute respiratory distress syndrome ($P = 0.052$) across the groups.
Conclusions: REBOA is a useful adjunct in supporting central perfusion during hemorrhagic shock; however, increasing occlusion time and shock results in a greater IL 6 release. Clinicians must anticipate inflammation mediated organ failure in post REBOA use patients.

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1. Introduction

Hemorrhage remains the leading cause of potentially preventable death in civilian [1,2] and military [3,4] trauma, with a significant proportion occurring before hospital admission [5,6]. Hemorrhage arising from the noncompressible regions in the torso and junctional regions has been consistently identified as particularly lethal with a mortality of 18%—50% [7—9].

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1. REPORT DATE **01 OCT 2014**	2. REPORT TYPE **N/A**	3. DATES COVERED **-**

4. TITLE AND SUBTITLE **The Inflammatory Sequelae of Aortic Balloon Occlusion in Hemorrhagic Shock**	5a. CONTRACT NUMBER
	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) **Morrison J. J., Ross J. D., Spencer J. R., Rasmussen T. E.,**	5d. PROJECT NUMBER
	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX**	8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT **Approved for public release, distribution unlimited**

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT **UU**	18. NUMBER OF PAGES **9**	19a. NAME OF RESPONSIBLE PERSON
a. REPORT **unclassified**	b. ABSTRACT **unclassified**	c. THIS PAGE **unclassified**			

Definitive hemorrhage control and resuscitation is crucial to survival from exsanguinating injury [10]. Despite advances in damage control resuscitation [11], most of the torso hemorrhage control interventions require hospital based facilities. However, the delivery of such care is both time dependent and capability driven; a patient must survive long enough to access such facility.

Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a proactive hemorrhage control adjunct designed to sustain vital perfusion until definitive hemostasis can be achieved [12,13]. In the setting of noncompressible torso hemorrhage, a balloon is inflated in the thoracic aorta. This augments cardiac afterload improving myocardial and cerebral perfusion while simultaneously controlling arterial inflow. Importantly, unlike resuscitative thoracotomy and aortic clamping, REBOA can be initiated without the need for general anesthesia and applied in resource poor environments.

Translational large animal work and early clinical series have shown REBOA to have significant promise as a bridge to definitive hemostasis [14–17]. However, this technique is known to incur a lactate penalty that is proportional to the length of occlusion. Although up to 90 min of occlusion has been demonstrated to be survivable in a swine model of hemorrhagic shock, the systemic inflammatory response and the cardiopulmonary sequelae have yet to be characterized [14]. The aim of this study was to quantify the inflammatory response to different occlusion times and their effect on cardiopulmonary function.

2. Methods

2.1. Overview

This study represents the analysis of previously unpublished data from three experimental groups (30 REBOA, n   6; 60 REBOA, n   8, and 90 REBOA, n   6) drawn from two previously published studies [14,15]. These two studies shared a common experimental design but realized different end points. All experiments were conducted at a single accredited large animal facility under the supervision of an Institutional Animal Care and Use Committee supported by licensed veterinary staff. All animals were in good health and housed for at least 7 d before study enrollment to allow for acclimation.

Female Yorkshire swine (*Sus scrofa*) weighing 70–90 kg were entered into a study protocol consisting of the following five phases: animal preparation, induction of hemorrhagic shock (30 min), balloon occlusion (30, 60, or 90 min), resuscitation (6 h), and critical care (48 h) (Fig. 1). Indices of hemodynamic performance were recorded throughout the study, along with blood sampling at specific time points. Animals were euthanized at the end of the critical care phase and necropsy performed.

2.2. Animal preparation

General anesthesia was induced using intravenous ketamine and maintained following orotracheal intubation with isoflurane (range 2%–4%). Animals were ventilated using a volume controlled mode of 6–8 mL/kg with an FiO_2 of 40%–80% sufficient to maintain an SpO_2 of >96%. Surgical exposure and cannulation of the common carotid, internal and external jugular vein was performed via a midline neck incision. This facilitated invasive blood pressure monitoring, intravenous fluid resuscitation, and the placement of a Swan Ganz catheter. A 14F sheath was placed in the external iliac artery via a retroperitoneal surgical exposure in the 30 and 90 REBOA groups, whereas this was accomplished in the 60 REBOA group by an ultrasound guided percutaneous technique.

A cerebral oximetry probe (LICOX; Integra LifeSciences, Plainsboro, NJ) and carotid flow probe (Transonic Systems Inc, Ithaca, NY) were also placed; the data from these devices have been reported previously and will not be discussed further.

2.3. Induction of hemorrhagic shock (30 min)

Class IV hemorrhagic shock was induced using a standardized technique previously described [18]. Over 20 min, 35% of the animal's blood volume (total porcine blood volume: 66 mL/kg) was removed from the iliac arterial sheath: half over 7 min and the remaining over 13 min. As the swine has a contractile spleen, animals underwent a further hemorrhage of 0.15 mL/kg/min for 10 min to minimize the effect of autotransfusion. Whole blood was collected in citrated bags for reinfusion during the resuscitation phase.

2.4. Balloon occlusion (30, 60, or 90 min)

Following the conclusion of the controlled hemorrhage, REBOA was performed either for 30, 60, or 90 min. A stiff Amplatz wire was passed through the 14F sheath into the thoracic aorta guided by fluoroscopy. A Coda balloon catheter (Cook Medical, Bloomington, IN) was advanced to the midpoint of the thoracic aorta using an "over the wire" technique and inflated with a mixture of saline and contrast medium observed under fluoroscopy.

2.5. Resuscitation (6 h) and critical care (48 h)

Fluid resuscitation was initiated 10 min before commencing balloon deflation at the end of the occlusion period (30, 60, or 90 min). Shed whole blood was slowly infused to raise the mean arterial pressure (MAP) by around 25%. This was to avoid precipitous cardiovascular collapse once balloon deflation was commenced, which was performed gradually over 3 min in parallel with the rapid infusion of shed whole blood. Once the balloon was fully deflated, the catheter and wire were withdrawn from the sheath.

Whole blood resuscitation continued and was titrated to an MAP of 60 mm Hg. Once these reserves were exhausted, boluses of 1.0 L of 0.9% saline were used to achieve the target blood pressure. When animals became refractory to fluid challenges, an infusion of norepinephrine was commenced at 4 μg/h and titrated to an MAP of 60 mm Hg. Animals were also transitioned from inhaled isoflurane to intravenous ketamine and midazolam sedation once considered sufficiently stable.
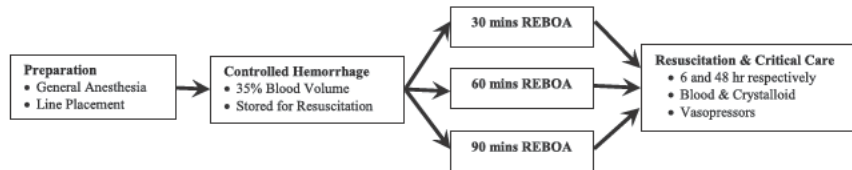
Fig. 1 — An overview of the experimental design.

2.6. Study end points, data collection and analysis

The primary outcomes of this study related to the rise in the proinflammatory cytokines are interleukin 6 (IL 6) and tumor necrosis factor alpha (TNF α). Serum samples were analyzed using an enzyme linked immunosorbent assays technique. IL 6 and TNF α were run on porcine specific kits obtained from R&D Systems (Minneapolis, MN). Plates were set up following manufacturer's instructions, read on a Bio Tek (Winooski, VT) Synergy H4 microplate reader and data analyzed using GEN5 software from Bio Tek.

Secondary outcomes related to measures of inflammation mediated cardiopulmonary dysfunction manifest as failure of vascular tone and the development of acute respiratory distress syndrome (ARDS). Failure of vascular tone was quantified by the need for vasopressor medication (norepi nephrine). Evidence of ARDS was made using the Berlin defi nition, which describes a mild, moderate, and severe pattern based on a $PaO_2:FiO_2$ ratio of 201—300, 100—200, and <100 mm Hg, respectively [19]. A pulmonary arterial wedge pressure (PAWP) of <18 mm Hg was used as an objective measure of the absence of cardiac failure, and histologic evidence of pulmo nary edema was used in lieu of chest radiography.

Indices of hemodynamic performance (cardiac output [CO], systemic vascular resistance [SVR], MAP, and PAWP) were recorded continuously throughout the study. Inflammatory cytokines were measured at 8 and 24 h. At the end of study, animals were euthanized, lungs removed, weighted, and sub mitted for blinded histologic evaluation by a veterinary pathologist.

Data were analyzed using SPSS version 20.0 (IBM, Chicago, IL). Chi square tests were used to compare categorical data and analysis of variance with *post hoc* testing for continuous variables using a Bonferroni correction.

3. Results

3.1. Baseline characteristics and induction of hemorrhagic shock

There was no significant difference in baseline measures of weight and hemodynamic or metabolic parameters between the 30 , 60 , or 90 REBOA groups (Table 1). The induction of shock was successful, with all animals tolerating the controlled hemorrhage well, achieving their predicted vol ume. Importantly, all animals demonstrated an appropriate tachycardia along with profound hypotension consistent with severe hypovolemic shock (Table 1). There was no unexpected mortality during the study protocol.

Table 1 — Baseline characteristics of the three study groups and physiology following a 35% controlled hemorrhage. Data are presented as mean and standard deviation or proportions (percentages).

Parameter	30 REBOA	60 REBOA	90 REBOA	P*
N	6	8	6	
Weight, kg	81.3 ± 7.5	77.5 ± 5.9	88.0 ± 11.3	0.143
Female, %	6 (100.0)	8 (100)	6 (100.0%)	N/A
Hemodynamic				
HR, bpm	80 ± 4	81 ± 8	76 ± 15	0.647
MAP, mm Hg	68 ± 11	65 ± 10	72 ± 8	0.447
SV, mL/min	91 ± 15	97 ± 22	73 ± 25	0.138
CO, L/min	7.2 ± 1.3	7.9 ± 1.6	6.4 ± 1.2	0.190
SVR, dynes.sec/cm^5	683 ± 120	607 ± 91	918 ± 125	<0.001
MPAP, mm Hg	17 ± 6	17 ± 4	20 ± 3	0.419
PAWP, mm Hg	11 ± 6	11 ± 4	12 ± 3	0.785
$FiO_2:PaO_2$ ratio, mm Hg	507 ± 130	467 ± 33	430 ± 188	0.571
Metabolic				
Temp, °C	35.3 ± 0.9	34.9 ± 1.3	35.6 ± 0.9	0.437
pH	7.47 ± 0.04	7.50 ± 0.03	7.44 ± 0.05	0.032
Lactate, mmol/L	1.3 ± 0.4	0.8 ± 0.2	1.2 ± 0.4	0.052
Hemorrhage				
Predicted volume, mL	2145 ± 197	2072 ± 174	2323 ± 300	0.144
Actual volume, mL	1996 ± 193	1942 ± 278	2264 ± 283	0.082
HR posthemorrhage, mm Hg	151 ± 26	167 ± 15	140 ± 23	0.073
MAP posthemorrhage, mm Hg	31 ± 4	35 ± 8	38 ± 13	0.433

HR = heart rate; MPAP = mean pulmonary arterial pressure; SV = stroke volume.
*Statistical test analysis of variance.

3.2. Hemodynamic performance and resuscitation

All groups responded to aortic occlusion with a substantial rise in MAP, which was sustained throughout each groups' respective occlusion period (Fig. 2A). A similar trend was noted with the SVR, which demonstrated a modest increase during the hemorrhage phase, but more than doubled after aortic balloon occlusion (Fig. 2B). This is in contrast to CO, which decreased during the hemorrhage phase entering a plateau during the balloon occlusion phase (Fig. 2C). It was only during the resuscitation phase did the CO increase, achieving similar values to the baseline recordings.

At the end of the study, there was no significant difference among the groups in the final heart rate, MAP, stroke volume, CO, mean pulmonary arterial pressure, PAWP, temperature, pH, or lactate measurements (Table 2). The SVR was significantly elevated in the 90 REBOA group compared with the 60 REBOA group (1189 ± 391 versus 623 ± 113; P 0.024). There were no significant differences in cardiac troponin I measured at 8 and 24 h (Table 2).

Regarding fluid resuscitation, all animals had their previously shed whole blood returned. The 60 REBOA group went on to receive a larger volume of crystalloid than the 30 REBOA group (12,014 ± 6699 versus 6535 ± 2517; P 0.043) and the 90 REBOA group (12,014 ± 6699 versus 10341 ± 7231; P 0.089), although the latter was not statistically significant (Table 2).

3.3. Inflammatory cytokines

There was no significant difference in baseline IL 6 (Fig. 3A; P 0.095) or TNF α (Fig. 4A; P 0.597) within the three groups. There was no significant increase in IL 6 compared with baseline value for the 8 and 24 h samples in the 30 REBOA group. By contrast, both the 60 and 90 REBOA groups saw a rise in IL 6 (picogram per milliliter) at 8 h compared with the baseline values: 289 ± 258 versus 10 ± 5; P 0.018 and 630 ± 348; P 0.007, respectively. This had returned to base line in the 60 REBOA group by 24 h (36 ± 36 versus 9 ± 6; P 0.083) but was still elevated in the 90 REBOA group (89 ± 45 versus 19 ± 20; P 0.028).

When examining between groups at 8 h, the 90 REBOA group has a significantly elevated IL 6 compared with the 30 REBOA group (630 ± 348 versus 53 ± 37; P 0.003; Fig. 3B). At 24 h, IL 6 in the 90 REBOA group was significantly greater compared with both the 30 and 60 REBOA groups: 89 ± 45 versus 16 ± 15; P 0.006 and 89 ± 45 versus 36 ± 36; P 0.040, respectively (Fig. 3C).

For TNF α, there was no significant elevation across the time points or among the groups (Fig. 4A−C).

3.4. Cardiopulmonary dysfunction

There was no statistical difference in either the total dose of norepinephrine or proportion of animals requiring
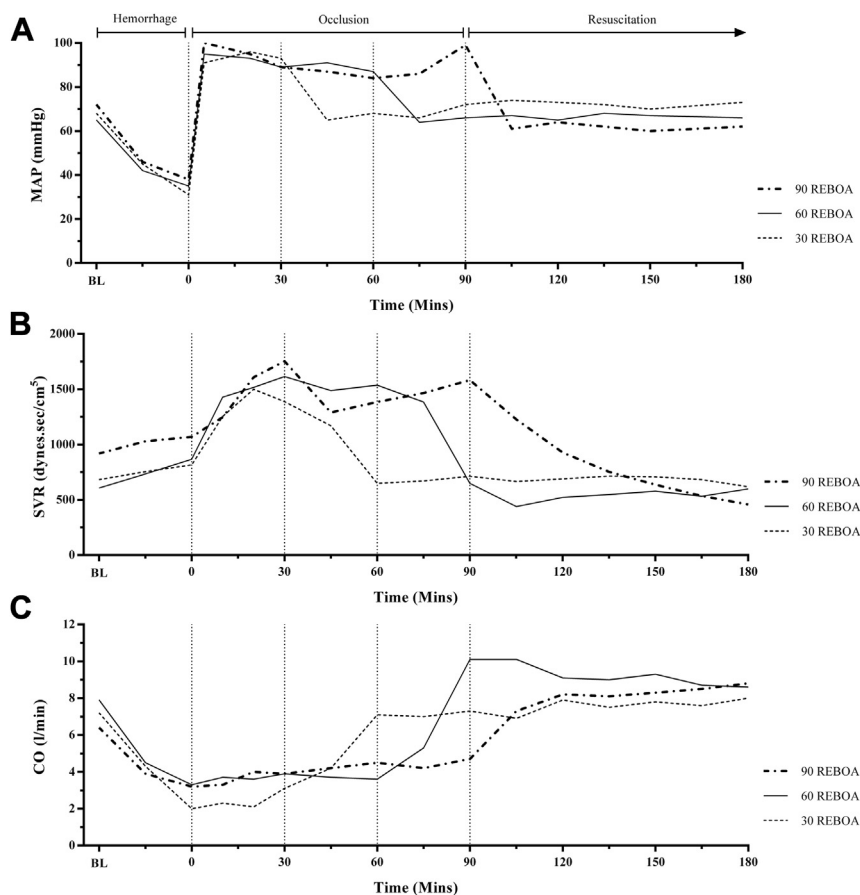

Fig. 2 − The hemodynamic performance of swine undergoing a controlled hemorrhage (35% circulating volume) and 30, 60, or 90 min of REBOA. Data are plotted as mean value. (A) MAP (B) SVR (C) CO.

Table 2 – End of study resuscitation volumes, hemodynamic indices, and metabolic and troponin measurements following 30, 60, or 90 min of aortic balloon occlusion. Data are presented as mean and standard deviation.

Parameter	30 REBOA	60 REBOA	90 REBOA	P*
N	6	8	6	
Hemodynamic				
HR, bpm	79 ± 18	102 ± 28	92 ± 10	0.163
MAP, mm Hg	78 ± 13	68 ± 14	86 ± 9	0.057
SV, mL/min	75 ± 22	87 ± 22	57 ± 6	0.129
CO, L/min	5.5 ± 1.6	6.0 ± 2.5	5.0 ± 1.0	0.765
SVR, dynes.sec/cm^5	977 ± 176	623 ± 113	1189 ± 391	0.003
MPAP, mm Hg	18 ± 7	21 ± 3	26 ± 6	0.096
PAWP, mm Hg	13 ± 7	10 ± 4	13 ± 9	0.666
FiO$_2$:PaO$_2$ ratio, mm Hg	516 ± 122	412 ± 124	313 ± 137	0.043
Metabolic				
Temp, °C	37.8 ± 1.3	37.8 ± 0.5	36.9 ± 1.2	0.268
pH	7.46 ± 0.02	7.40 ± 0.10	7.43 ± 0.04	0.298
Lactate, mmol/L	0.5 ± 0.1	0.6 ± 0.2	0.6 ± 0.1	0.440
Cardiac troponin I				
8 h, ng/mL	0.65 ± 0.46	0.87 ± 0.72	0.96 ± 0.80	0.719
24 h, ng/mL	0.28 ± 0.24	0.44 ± 0.38	0.38 ± 0.49	0.759
Total fluid resuscitation				
Whole blood, mL	1996 ± 193	1942 ± 278	2264 ± 283	0.082
Crystalloid, mL	6535 ± 2517	$12,014 \pm 6699$	$10,341 \pm 7231$	<0.001

HR = heart rate; MPAP = mean pulmonary arterial pressure; SV = stroke volume.
*Statistical test analysis of variance.

vasopressor support. These measures did however demonstrate a trend toward a stepwise increase in the vasopressor requirements across the 30 , 60 , and 90 REBOA groups. This was demonstrated by total dose (milligram) of norepinephrine administered (0.06 ± 0.09 versus 1.16 ± 2.58 versus 2.38 ± 2.31; P 0.183) and the proportion of animals requiring vasopressor support (2 [33.3%] versus 4 [50.0%] versus 5 (83.3%); P 0.205), respectively (Fig. 5A and B).

There was a significant stepwise increase in the wet lung weight to body weight ratio between the three groups (10.8 ± 2.5 versus 13.0 ± 3.4 versus 16.8 ± 2.7; P 0.008; Fig. 6A). The lung weight ratio of the 90 REBOA group was significantly greater than the 30 REBOA group; P 0.006. The inverse of this trend was observed in the end of study FiO$_2$:PaO$_2$ ratio, which reduced as occlusion time increased (Table 2). The 90 REBOA FiO$_2$:PaO$_2$ ratio was significantly less than that of the 30 REBOA group (313 ± 137 versus 516 ± 122; P 0.040; Table 2).

The incidence in ARDS trended toward an increase across the groups (P 0.052; Fig. 6B). No animals in the 30 REBOA group had an FiO$_2$:PaO$_2$ ratio suggestive of ARDS. There were 3 animals (37.5%) in the 60 REBOA group with a reduced FiO$_2$:PaO$_2$ ratio and histology (Fig. 7A and B) consistent with mild ARDS. There were 4 animals (66.7%) in the 90 REBOA group with the evidence of ARDS: two with mild and two with medium grade ARDS.

4. Discussion

The present study is the first characterization of the systemic inflammatory response after aortic balloon occlusion and hemorrhagic shock. As the occlusion time increased, a greater release of IL 6 as measured at 8 and 24 h was observed. This was associated with a trend toward an increase in vasopressor
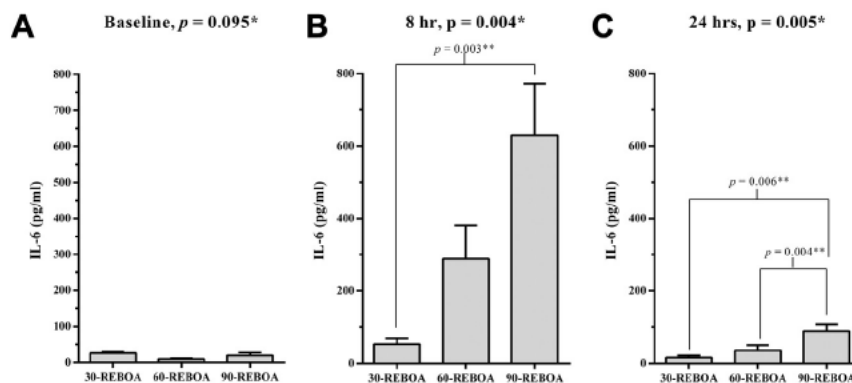

Fig. 3 – IL-6 measurements (mean and standard error) following 30, 60, and 90 min of hemorrhagic shock at (A) baseline, (B) 8 h and (C) 24 h *analysis of variance, **post hoc testing between groups.
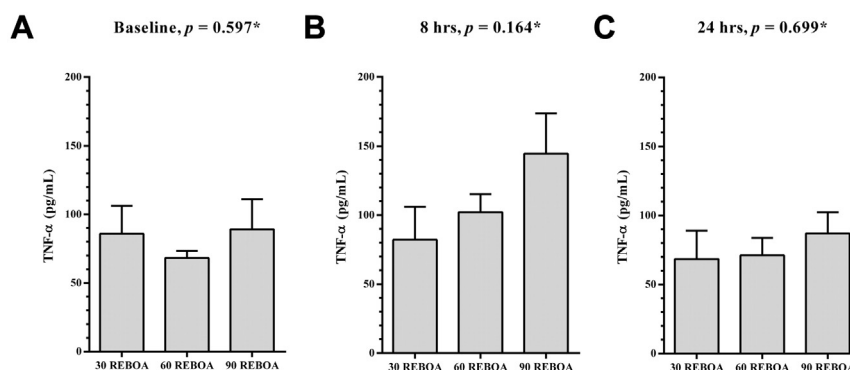
Fig. 4 — TNF-α measurements (mean and standard error) following 30, 60, and 90 min of hemorrhagic shock at (A) baseline, (B) 8 h and (C) 24 h *analysis of variance.

use and incidence of ARDS, which was unrelated to cardiac function as measured by a normal end of study PAWP and CO. The relationship between occlusion time and inflammatory sequelae is important in the understanding of the critical care challenges faced by the post REBOA patient.

The present study confirms and extends earlier work by White et al. [20], who compared REBOA to open thoracotomy and aortic clamp in porcine model of hemorrhagic shock. Although both methods of aortic occlusion demonstrated similarly favorable hemodynamic effect, the metabolic profile was significantly different. Clamp occlusion was associated with a significantly higher lactate burden and vasopressor requirement in comparison with REBOA. These investigators concluded that REBOA was superior to open thoracotomy and clamp occlusion in hemorrhagic shock, although further work was required to characterize the effect of REBOA.

Subsequently, Markov et al. [14] examined 30 and 90 min of hemorrhagic shock with and without balloon occlusion. Those investigators explored the influence of occlusion on measures of perfusion and demonstrated superior central pressures with balloon occlusion. This was associated with a significant metabolic burden as measured by serum lactate;

however, with suitable resuscitation, this returned to baseline levels within 6 h of occlusion.

Scott et al. [15] used an occlusion time of 60 min with which to evaluate a novel, self centering, low profile, prototype REBOA catheter compared with a conventional balloon system. This demonstrated the reproducibility of fluoroscopy free placement while examining the consequence of 60 min of occlusion. This also reaffirmed the favorable hemodynamic performance of balloon occlusion in shock on central perfusion.

The lactate burden reported in these studies demonstrates that REBOA was associated with a significant ische mia—reperfusion injury. The present study is able to explore this phenomenon in more detail, both using molecular markers and clinically relevant secondary endpoints. Impor tantly, by using a similar methodology in earlier studies, this has been achieved without the need for further animal experimentation. However, because of the nature of how the present study was constructed, there are some important limitations to discuss.

Several secondary endpoints did not achieve statistical significance, specifically, the total dose and proportion of an imals requiring vasopressor support. The finding that most of
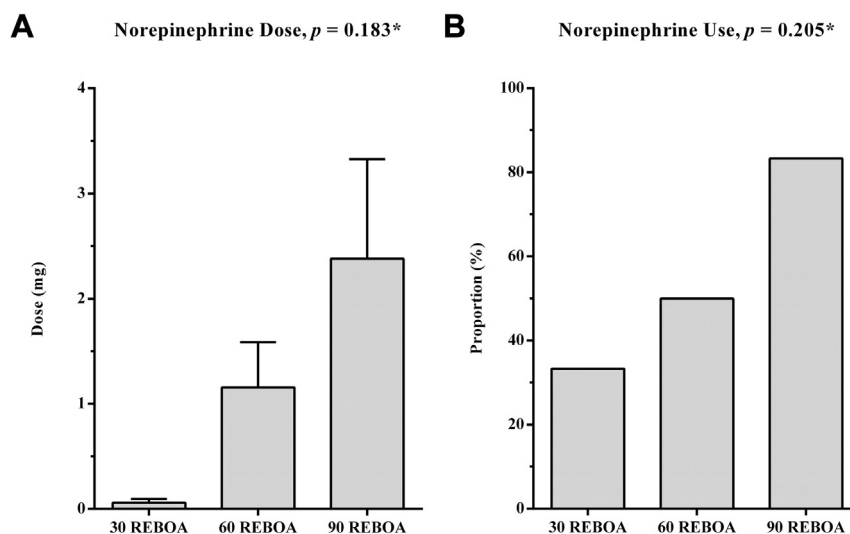

Fig. 5 — Total dose of norepinephrine (mean and standard deviation) and the proportion of animals requiring vasopressor support (percentage). (A) total dose and (B) proportion. *analysis of variance.
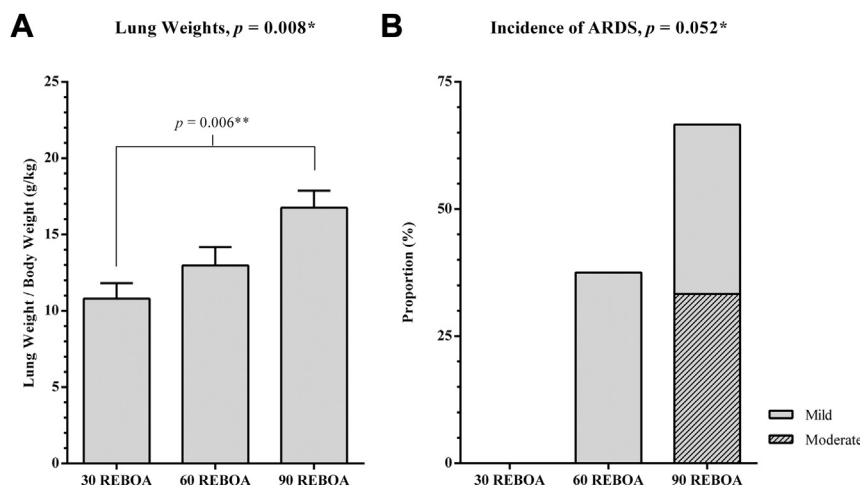
Fig. 6 — Measures of pulmonary congestion. (A) Lung weight per body weight (mean and standard error) and (B) incidence of ARDS. *analysis of variance, **_post hoc_ testing between groups.

the animals (80%) undergoing 90 min of occlusion required vasopressor support is clinically very important, although not reflected statistically. This likely relates to sample size.

Furthermore, there are some subtle differences in meth odology between the groups. Iliac arterial access was obtained percutaneously in the 60 REBOA group, whereas an operative approach was used in the 30 and 90 REBOA groups. The latter approach could increase soft tissue injury and artificially add to the inflammatory release, although the data presented here do not suggest that to be the case.

It is also important to discuss the resuscitation used, which was predominantly crystalloid based following the infusion of shed whole blood. A more "hemostatic" resuscitation (i.e., more blood products and less synthetic fluid) would have been preferable; however, this would have required a porcine blood bank, and the complexities inherent to such a capability. This is important, as significant crystalloid use has been associated with an increase in ARDS in trauma patients [21]. However, the IL 6 increase did not correlate with resuscitation volumes, suggesting that shock and aortic occlusion time contributes more to the generation of the systemic inflammatory response.

There was a greater volume of fluid resuscitation admin istered to the 60 REBOA group, which is surprising in the context of a common resuscitation protocol. This is likely reflective of differences between laboratory staff who per formed the experiments. It appears that the investigators in 60 REBOA group were more liberal in their fluid administration.

Finally, the present study does not include "control" groups consisting of hypovolemic shock without REBOA or normovo lemia with REBOA. This was deliberate, as the aim of the study was to explore the inflammatory burden associated with increasing occlusion times, not the effect of shock or REBOA alone. The effect of shock is already well characterized in the literature and the use of REBOA in normovolemia is not a clinically realistic scenario. Importantly, as REBOA is already in limited clinical use [17], it is crucial to examine relevant models.

Cytokines are well established mediators of inflammation and their excessive release is associated with multiple organ failure after trauma and sepsis [22—24]. The results noted in the present study support and extend the literature relating to cytokine release and traumatic injury. IL 6 and TNF α have been noted to be elevated in both hemorrhage and tissue injury, although different mechanisms and time courses prevail [25,26].

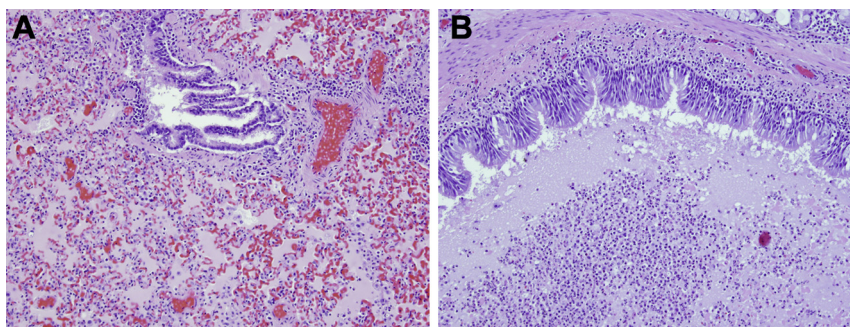**Fig. 7 — A representative histologic section of an animal that underwent 90 min of REBOA (hematoxylin and eosin stain, ×10 Magnification). (A) Diffuse severe alveolar edema. (B) bronchial exudates. These features, in conjunction with an FiO$_2$:PaO$_2$ ratio <300 mm Hg, are suggestive of ARDS (Color version of figure is available online). (Image courtesy of Dr ME Thompson, DVM, Dip ACVP and Mrs H Brown, 59th Medical Wing).**

TNF α has been associated with an early rise at 45 min, persisting up to 4 h in hemorrhage, whereas although IL 6 rises similarly, it tends to persist for longer and is more associated with tissue injury [26]. This may explain the discrepancy in trend between IL 6 and TNF α in the previously mentioned study. Unfortunately, because of the *post hoc* way in which the present study is constructed, serum for analysis from early post REBOA time points is unavailable. Further study is required to assess the role of other cytokine at different time points.

Within the context of the present study, IL 6 has been linked to the development of ARDS [27–31]. Several small animals studies have demonstrated that IL 6 produced in response to hemorrhage induces the sequestration of poly morphic neutrophils in the pulmonary capillary beds [32,33]. Interestingly, no animal in the present study demonstrated severe ARDS, suggesting that this may be a self limiting phenomenon, although further investigation is required.

REBOA is a proactive method of circulatory support designed to salvage patients with end stage hypovolemic shock, bridging their physiology until definitive hemorrhage control. However, it is important to note that this technique is still in its infancy and that the appropriate clinical niche has yet to be established. The military has a need for such an adjunct as a significant number of patient decompensate *en route* to definitive hemorrhage control due to extended pre hospital times [34].

The application of REBOA in the civilian environment is less clear, although it is now being gradually introduced into clinical practice with formalized protocols established in several civilian trauma systems. A number of successful case series have already been published demonstrating the clinical utility of REBOA in hemorrhagic shock [16,17]. Although these reports are promising, several hurdles need to be overcome. On a practical level, specialist training is required for REBOA providers, with experience in obtaining arterial access in hy potensive patient essential. Furthermore, as the present study demonstrates, critical care facilities must be available to the post REBOA patients to maintain physiological homeostasis postdeflation.

Clinicians need to be aware of the association between occlusion time and inflammatory burden. While clearly providers need to strive for the minimum occlusion time possible, the reality is that some patients with complex in juries will push that envelope. It is important that the use of REBOA does not simply transition the place of death from the ER to the ICU. It will be vital to anticipate the critical care needs of all patients who undergo REBOA, but especially so for those with extended occlusion time of 60 min and beyond.

Several promising lines of research have opened up that could potentially be combined with REBOA systems to help ameliorate the inflammatory burden of occlusion in shock. Technologies that can eliminate proinflammatory mediators, such as hemoadsorption filters [35], could be included within an extracorporeal circuit merged with a REBOA system. Equally, a perfusion capable REBOA catheter [36] could be used to prophylactically deliver an anti inflammatory perfusate such as a statin suspension [37].

5.   Conclusions

The present study reaffirms that in severe hemorrhagic shock, REBOA can help sustain central perfusion, despite a low car diac out, by increasing SVR. Importantly, there appears to be a minimal direct cardiac injury as a result of this hemodynamic mechanism. There is a proportional relationship between the length of shock and the resultant proinflammatory IL 6 release. This is associated with a trend toward an increase in vasopressor use and the incidence of ARDS, suggestive of a clinically important systemic inflammatory response. Clini cians must anticipate the need for organ support when managing patients where REBOA has been used as a hemor rhage control adjunct.

Acknowledgment

Disclosure

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